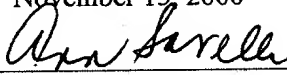


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Paul J. Carter Serial No.: not yet assigned Filed: November 15, 2000 For: EXPRESSION OF FUNCTIONAL ANTIBODY FRAGMENTS	Group Art Unit: not yet assigned Examiner: not yet assigned <div style="border: 1px solid black; padding: 5px;"> <p style="text-align: center; margin: 0;">CERTIFICATE OF EXPRESS MAILING</p> <p style="font-size: small; margin: 0;">I hereby certify that this correspondence is being deposited with the United States Postal Service "Post Office to Addressee" under 37 CFR 1.10 on the date indicated below and is addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231. Express Mail Label No. EL599584238 US</p> <p style="text-align: center; margin: 5px 0;">November 15, 2000</p> <p style="text-align: center; margin: 0;"> Ann Savelli</p> </div>
---	--

JCS31 U.S. PTO
 09/714040
 11/15/00

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Applicants submit herewith patents, publications or other information (attached hereto and listed on the attached Form PTO-1449) of which they are aware, which they believe may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 CFR §1.56.

This Information Disclosure Statement:

- (a) ☒ accompanies the new patent application submitted herewith. 37 CFR §1.97(a).
- (b) ☐ is filed within three months after the filing date of the application or within three months after the date of entry of the national stage of a PCT application as set forth in 37 CFR §1.491.
- (c) ☐ as far as is known to the undersigned, is filed before the mailing date of a first Office action on the merits. Should any fee be due, the U.S. Patent and Trademark Office is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$240.00 to cover the cost of this Information Disclosure Statement. Any deficiency or overpayment should be charged or credited to this deposit account.
- (d) ☐ is filed after the first Office Action and more than three months after the application's filing date or PCT national stage date of entry filing but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and is accompanied by either the fee (\$240) set forth in 37 CFR §1.17(p) or a statement as specified in 37 CFR §1.97(e), as checked below. Should any fee be due, the U.S. Patent and Trademark Office is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$240.00 to cover the cost of this Information Disclosure Statement. Any deficiency or overpayment should be charged or credited to this deposit

account. **A duplicate of this sheet is enclosed.**

- (e) ☐ is filed after the mailing date of either a final rejection or a notice of allowance, whichever occurred first, and is accompanied by the fee (\$130) set forth in 37 CFR §1.17(i) and a statement as specified in 37 CFR §1.97(e), as checked below. **This document is to be considered as a petition requesting consideration of the information disclosure statement.** The U.S. Patent and Trademark Office is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$130.00 to cover the cost of this Information Disclosure Statement. Any deficiency or overpayment should be charged or credited to this deposit account. **A duplicate of this sheet is enclosed.**

[If either of boxes (d) or (e) is checked above, the following statement under 37 CFR §1.97(e) may need to be completed.] The undersigned states that:

- ☐ Each item of information contained in the information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.

A list of the patent(s) or publication(s) is set forth on the attached Form PTO-1449 (Modified).

A copy of the items on PTO-1449 is supplied herewith:

- ☐ each ☒ none ☐ only those listed below:

Those patent(s) or publication(s) which are marked with an asterisk (*) in the attached PTO-1449 form are not supplied because they were previously cited by or submitted to the Office in a prior application Serial No. 08/199,268, filed February 28, 1994 and relied upon in this application for an earlier filing date under 35 USC §120.

- ☐ BLAST results enclosed:

The undersigned also wishes to bring to the attention of the Examiner BLAST results of computerized alignments of the against sequences contained in the GenBank and Dayhoff databases. The BLAST results are provided in paper form and are identified as reference "BLAST Results A-1- A-0" (GenBank) and "BLAST Results B-1 - B-0" (Dayhoff) on the PTO Form 1449. Applicant requests that these references also be considered and that the Form 1449 be initialed to indicate the Examiner's consideration of the references.

A concise explanation of relevance of the items listed on PTO-1449 is:

- ☒ not given

- ☐ given for each listed item

- ☐ given for only non-English language listed item(s) [Required]
- ☐ in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references.

The Examiner is reminded that a "concise explanation of the relevance" of the submitted prior art "may be nothing more than identification of the particular figure or paragraph of the patent or publication which has some relation to the claimed invention," MPEP §609.

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR §1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

In accordance with 37 CFR §1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR §1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR §1.98 and MPEP §609 and the Examiner is respectfully requested to consider the listed references.

Respectfully submitted,
GENENTECH, INC.

Date: November 15, 2000

By: 

Wendy M. Lee
Reg. No. 40,378

1 DNA Way
So. San Francisco, CA 94080-4990
Phone: (650) 225-1994
Fax: (650) 952-9881

FORM PTO-1449

U.S. Dept. of Commerce
Patent and Trademark OfficeAtty Docket No.
P0710P1D1Serial No.
not yet assigned

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)

Applicant
CarterFiling Date
15 Nov 2000Group
not yet assigned

U.S. PATENT DOCUMENTS

Examiner Initials		Document Number	Date	Name	Class	Subclass	Filing Date
	* 1	4,444,878	24.04.84	Paulus et al.			05.12.83
	* 2	4,642,334	10.02.87	Moore et al.			
	* 3	4,816,567	28.03.89	Cabilly et al.			
	* 4	4,946,778	07.08.90	Ladner et al.			03.07.89
	* 5	5,219,966	15.06.93	Bodmer, et al.			29.04.94
	* 6	5,618,920	08.04.97	Robinson et al.			03.05.95
	* 7	5,648,237	15.07.97	Carter, P.			
	* 8	5,698,417	16.12.97	Robinson et al.			
	* 9	5,698,435	16.12.97	Robinson et al.			

JCS31 U.S. PTO
 09/714040
 11/15/00

FOREIGN PATENT DOCUMENTS

Examiner Initials		Document Number	Date	Country	Class	Subclass	Translation Yes	No
	*10	AU-A-27617/88	07.06.89	AUSTRALIA				
	*11	AU-B-57621/90	03.01.91	AUSTRALIA				
	*12	0338745	25.10.89	EPO				
	*13	136,907	10.04.85	EPO				
	*14	459,577	04.12.91	EPO				
	*15	WO 89/01783	09.03.89	PCT				
	*16	WO 89/01974	09.03.89	PCT				
	*17	WO 89/06692	27.07.89	PCT				
	*18	WO 92/01059	23.01.92	PCT				
	*19	WO 92/10209	25.06.92	PCT				
	*20	WO 92/22324	23.12.92	PCT				
	*21	WO 93/12220	24.06.93	PCT				

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

	*22	Axelsson K., "Bacterial Lipopolysaccharides and Glutathione Mixed Disulfides as Possible Contaminants of Human Growth Hormone Produced with the Use of E. coli K12" <u>Acta Chemica Scandinavica, Series B</u> 39(1):69-77 (1985)
	*23	Better and Horwitz, "Expression of engineered antibodies and antibody fragments in microorganisms" <u>Methods in Enzymology</u> 178:476-496 (1989)
	*24	Better et al., "Escherichia coli secretion of an active chimeric antibody fragment" <u>Science</u> 240:1041-1043 (1988)
	*25	Better et al., "Potent anti-CD5 ricin A chain immunoconjugates from bacterially produced Fab' and F(ab') ₂ " <u>Proc. Natl. Acad. Sci. USA</u> 90:457-461 (1993)
	*26	Better et al., "Production and Scale Up of Chimeric Fab Fragments from Bacteria" <u>Advances in Gene Technology: The Molecular Biology of Immune Diseases & the Immune Response</u> (ICSU Short Rpts.), Streilein et al., eds. Vol. 10:105 (1990)
	*27	Bird et al., "Single-chain antigen-binding proteins" <u>Science</u> 242:423-426 (Oct 1988)

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. Dept. of Commerce
Patent and Trademark OfficeAtty Docket No.
P0710P1D1Serial No.
not yet assignedApplicant
CarterFiling Date
15 Nov 2000Group
not yet assigned

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

- | | |
|-----|---|
| *28 | Boss et al., "Assembly of functional antibodies from immunoglobulin heavy and light chains synthesised in <i>E. coli</i> " <u>Nucleic Acids Research</u> 12(9):3791-3806 (1984) |
| *29 | Brennan et al., "Preparation of bispecific antibodies by chemical recombination of monoclonal immunoglobulin G ₁ fragments" <u>Science</u> 229:81-83 (July 1985) |
| *30 | Burgess et al., "Possible Dissociation of the Heparin-binding and Mitogenic Activities of Heparin-binding (Acidic Fibroblast) Growth Factor-1 from Its Receptor-binding Activities by Site-directed Mutagenesis of a Single Lysine Residue" <u>Journal of Cell Biology</u> 111:2129-2138 (1990) |
| *31 | Cabilly et al., "Generation of Antibody Activity from Immunoglobulin Polypeptide Chains Produced in <i>Escherichia coli</i> " <u>Proc. Natl. Acad. Sci. USA</u> 81:3273-3277 (1984) |
| *32 | Cabilly, Shmuel, "Growth at sub-optimal temperatures allows the production of functional, antigen-binding Fab fragments in <i>Escherichia coli</i> " <u>Gene</u> 85:553-557 (1989) |
| *33 | Carter et al., "High level <i>Escherichia coli</i> expression and production of a bivalent humanized antibody fragment" <u>Bio/Technology</u> 10:163-167 (1992) |
| *34 | Carter et al., "Humanization of an anti-p185HER2 antibody for human cancer therapy" <u>Proc. Natl. Acad. Sci.</u> 89:4285-4289 (May 1992) |
| *35 | Carter, P. and Wells, J.A., "Engineering enzyme specificity by "substrate-assisted catalysis"" <u>Science</u> 237:394-399 (1987) |
| *36 | Chothia et al., "Domain Association in Immunoglobulin Molecules. The Packing of Variable Domains" <u>Journal of Molecular Biology</u> 186:651-663 (1985) |
| *37 | Condra et al., "Bacterial expression of antibody fragments that block human rhinovirus infection of cultured cells" <u>Journal of Biological Chemistry</u> 265(4):2292-2295 (1990) |
| *38 | Cumber et al., "Comparative stabilities in vitro and in vivo of a recombinant mouse antibody FvCys fragment and a bisFvCys conjugate" <u>J. Immunol.</u> 149(1):120-126 (1992) |
| *39 | Fanger et al., "Bispecific antibodies and targeted cellular cytotoxicity" <u>Immunology Today</u> 12(2):51-54 (1991) |
| *40 | Fendly et al., "Characterization of Murine Monoclonal Antibodies Reactive to Either the Human Epidermal Growth Factor Receptor or HER2/neu Gene Product" <u>Cancer Research</u> 50:1550-1558 (Mar 1, 1990) |
| *41 | Gavit et al., "Purification of a Mouse-Human Chimeric Fab Secreted from <i>E. coli</i> " <u>BioPharm</u> pps. 28-29, 32-34, 58 (1992) |
| *42 | Gilles et al., "Antigen binding and biological activities of engineered mutant chimeric antibodies with human tumor specificities" <u>Hum. Antibod. Hybridomas</u> 1(1):47-54 (1990) |
| *43 | Glennie et al., "Preparation and Performance of Bispecific F(ab') ₂ Antibody Containing Thioether-Linked Fab'γ Fragments" <u>J. Immunol.</u> 139(7):2367-2375 (October 1, 1987) |
| *44 | Glennie M.J. et al., "Bispecific F(ab') ₂ antibody for the delivery of saporin in the treatment of lymphoma" <u>J. Immunol.</u> 141(10):3662-3670 (1988) |
| *45 | Glockshuber et al., "A Comparison of Strategies to Stabilize Immunoglobulin Fv-Fragments" <u>Biochemistry</u> 29:1362-1367 (1990) |
| *46 | Hammerling et al., "Use of hybrid antibody with anti-γG and anti-ferritin specificities in locating cell surface antigens by electron microscopy" <u>Journal of Experimental Medicine</u> 128:1461-1469 (1968) |
| *47 | Hasemann and Capra, "High-level production of a functional immunoglobulin heterodimer in a baculovirus expression system" <u>Proc. Natl. Acad. Sci. USA</u> 87:3942-3946 (1990) |

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		U.S. Dept. of Commerce Patent and Trademark Office		Atty Docket No. P0710P1D1	Serial No. not yet assigned
LIST OF DISCLOSURES CITED BY APPLICANT (Use several sheets if necessary)				Applicant Carter	
				Filing Date 15 Nov 2000	Group not yet assigned
OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)					
*48	Hashida et al., "More Useful Maleimide Compounds for the Conjugation of Fab' to Horseradish Peroxidase Through Thiol Groups in the Hinge" <u>Journal of Applied Biochemistry</u> 6:56-63 (1984)				
*49	Horwitz et al., "Secretion of functional antibody and Fab fragment from yeast cells" <u>Proc. Natl. Acad. Sci. USA</u> 85:8678-8682 (1988)				
*50	Hudziak et al., "p185 ^{HER2} Monoclonal Antibody Has Antiproliferative Effects In Vitro and Sensitizes Human Breast Tumor Cells to Tumor Necrosis Factor" <u>Molecular & Cellular Biology</u> 9(3):1165-1172 (Mar 1989)				
*51	Huse et al., "Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda" <u>Science</u> 246:1275-1281 (1989)				
*52	Huston et al., "Protein engineering of antibody binding sites: Recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli" <u>Proc. Natl. Acad. Sci. USA</u> 85:5879-5883 (Aug 1988)				
*53	Johnstone et al. <u>Immunochemistry in Practice</u> , Blackwell Scientific Publications pps. 52-60 (1982)				
*54	Jungbauer et al., "Pilot scale production of a human monoclonal antibody against human immunodeficiency virus HIV-1" <u>Journal of Biochemical and Biophysical Methods</u> 19:223-240 (1989)				
*55	Kabat et al. <u>Sequences of Proteins of Immunological Interest</u> , Bethesda, MD:National Institutes of Health pps. iii-xxiii, 41-76 and 160-167 (1987)				
*56	King et al., "Tumor Localization of Engineered Antibody Fragments" <u>Antibody, Immunoconjugates, & Radiopharmaceuticals</u> 5(2):159-170 (1992)				
*57	Lazar et al., "Transforming Growth Factor α : Mutation of Aspartic Acid 47 and Leucine 48 Results in Different Biological Activities" <u>Molecular & Cellular Biology</u> 8(3):1247-1252 (Mar. 1988)				
*58	Liu et al., "Heteroantibody duplexes target cells for lysis by cytotoxic T lymphocytes" <u>Proc. Natl. Acad. Sci. USA</u> 82:8648-8652 (1985)				
*59	Lupu et al., "Direct interaction of a ligand for the erbB2 oncogene product with the EGF receptor and p185erbB2" <u>Science</u> 249:1552-1555 (1990)				
*60	Lyons et al., "Site-specific attachment to recombinant antibodies via introduced surface cysteine residues" <u>Protein Engineering</u> 3(8):703-708 (1990)				
*61	Mandy et al., "Recombination of Univalent Subunits Derived from Rabbit Antibody" <u>The Journal of Biological Chemistry</u> 236(12):3221-3226 (December 1961)				
*62	McCafferty et al., "Phage antibodies: filamentous phage displaying antibody variable domains" <u>Nature</u> 348:552-554 (1990)				
*63	Miller, S., "Protein-protein recognition and the association of immunoglobulin constant domains" <u>J. Mol. Biol.</u> 216:965-973 (1990)				
*64	Milstein et al., "Hybrid Hybridomas and Their Use in Immunohistochemistry" <u>Nature</u> 305:537-540 (1983)				
*65	Morrison et al., "Chimeric Human Antibody Molecules: Mouse Antigen-binding Domains with Human Constant Region Domains" <u>Proc. Natl. Acad. Sci. USA</u> 81:6851-6855 (November 1984)				
*66	Morrison et al., "Genetically Engineered Antibody Molecules and Their Application" <u>Biological Approaches to the Controlled Delivery of Drugs</u> , Annals of the New York Academy of Sciences, New York, New York: The New York Academy of Sciences Vol. 507:187-198 (1987)				
*67	Morrison et al., "Production and Characterization of Genetically Engineered Antibody Molecules" <u>Clinical Chemistry</u> 34(9):1668-1675 (1988)				
Examiner				Date Considered	
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

FORM PTO-1449 LIST OF DISCLOSURES CITED BY APPLICANT (Use several sheets if necessary)		U.S. Dept. of Commerce Patent and Trademark Office		Atty Docket No. P0710P1D1	Serial No. not yet assigned
				Applicant Carter	
				Filing Date 15 Nov 2000	Group not yet assigned
OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)					
*68	Neuberger et al., "Recombinant Antibodies Possessing Novel Effector Functions" <u>Nature</u> 312:604-608 (December 13, 1984)				
*69	Nikaido et al., "Outer Membrane" <u>Escherichia Coli and Salmonella Typhimurium</u> , Frederick C. Neidhardt, Washington, D.C.:American Society for Microbiology Vol. 1:7-21				
*70	Nisonoff and Mandy, "Quantitative estimation of the hybridization of rabbit antibodies" <u>Nature</u> 4826:355-359 (1962)				
*71	Nitta et al., "Preliminary trial of specific targeting therapy against malignant glioma" <u>Lancet</u> 335(8686):368-371 (Feb 17, 1990)				
*72	Nitta, T. et al., "Bispecific F(ab') ₂ monomer prepared with anti-CD3 and anti-tumor monoclonal antibodies is most potent in induction of cytolysis of human T cells" <u>European Journal of Immunology</u> 19:1437-1441 (1989)				
*73	Nolan et al., "Bifunctional antibodies: concept, production and applications" <u>Biochimica et Biophysica Acta</u> 1040:1-11 (1990)				
*74	Novotny et al., "Structural invariants of antigen binding: comparison of immunoglobulin V _L -V _H and V _L -V _L domain dimers" <u>Proc. Natl. Acad. Sci. USA</u> 82(14):4592-4596 (Jul 1985)				
*75	Padlan et al., "Antibody Fab assembly: the interface residues between CH1 and CL" <u>Molecular Immunology</u> 23(9):951-960 (1986)				
*76	Pantoliano et al., "Protein engineering of subtilisin BPN': Enhanced stabilization through the introduction of two cysteines to form a disulfide bond" <u>Biochemistry</u> 26:2077-2082 (1987)				
*77	Parham, "Preparation and purification of active fragments from mouse monoclonal antibodies" <u>Handbook of Experimental Immunology</u> , Weir E.M. (ed.), 4th edition, CA:Blackwell Scientific, Chapter 14, Vol. 1:14.1-14.23 (1986)				
*78	Parham, Peter, "In Vitro production of a hybrid monoclonal antibody that preferentially binds to cells that express both HLA-A2 and HLA-B7" <u>Human Immunology</u> 12:213-221 (1985)				
*79	Paulus, H., "Preparation and Biomedical Applications of Bispecific Antibodies" <u>Behring Inst. Mitt.</u> 78:118-132 (1985)				
*80	Perez et al., "Specific targeting of cytotoxic T cells by anti-T3 linked to anti-target cell antibody" <u>Nature</u> 316:354-356 (1985)				
*81	Pluckthun and Skerra, "Expression of functional antibody Fv and Fab fragments in Escherichia coli" <u>Methods in Enzymology</u> 178:497-515 (1989)				
*82	Pluckthun et al., "Engineering of antibodies with a known three-dimensional structure" <u>Cold Spring Harbor Symposia on Quantitative Biology</u> , Cold Spring Harbor Laboratory Vol. LII:105-112 (1987)				
*83	Pluckthun, Andreas, "Antibody engineering: advances from the use of escherichia coli expression systems" <u>Biotechnology</u> 9:545-51 (1991)				
*84	Putlitz et al., "Antibody production in baculovirus-infected insect cells" <u>Bio/Technology</u> 8:651-654 (1990)				
*85	Raso and Griffin, "Hybrid antibodies with dual specificity for the delivery of ricin to immunoglobulin-bearing target cells" <u>Cancer Research</u> 41:2073-2078 (1981)				
*86	Riechmann et al., "Expression of an Antibody Fv Fragment in Myeloma Cells" <u>J. Mol. Biol.</u> 203:825-828 (1988)				
*87	Rodrigues et al., "Engineering Fab' Fragments for Efficient F(ab) ₂ Formation in Escherichia coli and for Improved In Vivo Stability" <u>The Journal of Immunology</u> 151(12):6954-6961 (December 15, 1993)				
Examiner				Date Considered	
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

FORM PTO-1449

U.S. Dept. of Commerce
Patent and Trademark Office

Atty Docket No.

P0710P1D1

Serial No.

not yet assigned

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)

Applicant

Carter

Filing Date

15 Nov 2000

Group

not yet assigned

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

[illegible]

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.